Docket No. P16121

UNITED STATES PATENT AND TRADEMARK OFFICE

VERIFICATION OF A TRANSLATION

I, Charles Edward SITCH BA,

Deputy Managing Director of RWS Group plc UK Translation Division, of Europa House, Marsham Way, Gerrards Cross, Buckinghamshire, England hereby declare that:

My name and post office address are as stated below;

That the translator responsible for the attached translation is knowledgeable in the English language and in the Japanese language, and that, to the best of RWS Group plc knowledge and belief, the English translation of the attached Japanese document is true and complete.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: December 23, 2003

Signature : C.Sitch

For and on behalf of RWS Group plc

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England.

(Development Receipt No.: Received by: Date:)

Intellectual Property Legal Dept. Receipt No.:	Received by:	Date received by Intellectual Property Legal Dept.:	
Proposer of the Invention:	1. Title of the Invention (Provisional) High resolution scanning optical microscope in which clear images are produced at high speed		
Inventor (DISCLOSED BY INVENTOR:) Yoshihiro Kawano	Date: November 25, 2002	Inventor DISCLOSED BY INVENTOR:) Kiyoshi Koike	Date:

Inventors: Yoshihiro Kawano, Kiyoshi Koike

2. Draft of scope of the claims (Novel features include the following):

1. Scanning optical microscope, characterized in that it is configured from an illumination light source, a lens member necessary for altering the cross-sectional shape aspect ratio of the beam of light emitted from the light source, at least one lens for converging beams of light of different cross-sectional shape aspect ratio to create a linear light, a light modulation member able to impart shade to the converged linear light; at least one lens that can form the light to which the shade has been imparted as a parallel light, at least one scanning member that can alter the angle of illumination, at least one lens for imaging the light to which the shade has been imparted in one action, an objective lens that is employed to guide the light to which the shading has been imparted to a sample body, at least one lens necessary for imaging the reflected light from the sample body or the light generated by the sample body on to a line sensor, photographic element or light-receiving element, and a light-receiving element.

2. Scanning optical microscope of Claim 1, characterized in that a laser beam or a white light source such as a high-pressure mercury lamp, xenon lamp, halogen lamp or metal halide lamp is employed as the illumination light source.

3. Scanning optical microscope of Claim 1, characterized in that it comprises a light modulation member that can impart a confocal effect to light returned from the sample body, and the confocal effect can be changed or the confocal effect can be removed by alteration of the beam diameter or beam number of the light transmitted through the light modulation member.

4. Scanning optical microscope of Claim 1, characterized in that, if there is a desire to lower the confocal effect or to provide illumination of strong strength, by the provision of a function by which the surface area of the point on the light modulation member through which the light is transmitted and reflected

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is enlarged, or a simultaneous transmission and reflection thereof through the plurality of adjacent points is performed, the same effect as the effect obtained when a confocal diaphragm is opened can be produced.

5. Scanning optical microscope of Claim 1, characterized in that, by the use of a computer, the start and stopping operations of the scanning member and the regulation of the scanning speed thereof can be implemented, the illumination pattern of the light modulation member can be altered, and the ON/OFF irradiation of the illumination light on the sample body can be controlled.

6. Scanning optical microscope of Claim 1 in which a light modulation member for the purpose of imparting shade to a linear light, comprises any of the following members:
a diffraction grating characterized in that fringes are formed by the splitting of the laser beam into a plurality of beams and the interference of this plurality of beams by the diffraction grating and a lens necessary for the formation of these interference fringes, an optical member,
a DMD (Digital Mirror Device) characterized by the switching ON and OFF of small reflecting mirrors,
a one-dimensional mirror array,
a liquid crystal plate able to change the transmissivity, and
an SLM (spatial light modulator).

7. Scanning optical microscope of Claim 1, characterized in that a single-point illumination method confocal image is able to be produced by the control of the light modulation member in which the shade pattern is alterable and, by scanning with a galvanometer mirror, the illumination of the sample body by the timed shifting of a single-point illumination light to the position of illumination only.

8. Scanning optical microscope of Claim 1, characterized in that a plurality of points can be simultaneously illuminated on the sample body by the imparting of an alternating shade pattern to the light modulation member in which the shade pattern is alterable, and a confocal image can be produced by the alteration of this shade pattern and simultaneous illumination of a plurality of points.

9. Scanning optical microscope of Claim 1, characterized in that, employing a light modulation member in which the shade pattern is alterable, one segment of the visual field can be simultaneously illuminated and the sample body can be scanned with a linear light.

10. Scanning optical microscope of Claim 1, characterized in that the lens member necessary for altering the cross-sectional shape aspect ratio of the

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beam of the light emitted from the light source comprises one or more cylindrical lenses or one or more f θ lenses.

11. Scanning optical microscope of Claim 1, characterized in that the scanning member comprises a galvanometer mirror, polygon mirror or Acousto-Optic Modulator (AOM)

12. Scanning optical microscope of Claim 1, characterized in that the sample body is scanned several times by linear illumination lights of different shade pattern, and one image is produced from the plurality of scanned data.

13. Scanning optical microscope of Claim 1, characterized in that the laser beam is introduced through a fiber.

14. Scanning optical microscope of Claim 1, characterized in that, by virtue of the fact that most of the illumination light can be led to the sample body surface without restriction by the confocal diaphragm and, furthermore, the scanning of the scanning member can be implemented so as to illuminate the illumination light across the whole of the visual field, and, the reflected light and fluorescence and so on produced from the sample body can be projected on to the photographic element, the reflected light and fluorescence of the sample body can be observed.

15. Scanning optical microscope of Claim 1, characterized in that the illumination is performed using a titanium sapphire laser or another ultra-short pulse laser, and the fluorescence is able to be observed by multi-photon excitation such as two-photon excitation or three-photon excitation.

16. Scanning optical microscope of Claim 1, characterized in that the spectral diffraction device can be configured by the insertion of a diffraction grating that employs a prism, an Acousto-Optic Modulator (AOM) or spectral element between a photographic element that receives light from the sample body and a light strength modulating member, and the employment of a two-dimensional photographic element as the photographic element.

17. Scanning optical microscope of Claim 1, characterized in that non-linear light generated from the sample body, by way of example, secondary harmonic, tertiary harmonic, Raman light and CARS (Coherent Anti-Stokes Raman Scattering) can be received.

18. Scanning optical microscope of Claim 1 in which a two-dimensional photographic element is employed as the light-receiving element. Examples of the two-dimensional photographic element include a high sensitivity cooled CCD camera, back-illuminated CCD camera or cascade camera, as well as a CCD camera with an image intensifier.

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19. Scanning optical microscope of Claim 1 in which a line sensor is employed as the light-receiving element. Examples of the line sensor include a photo diode array, a PMT array and a line CCD array.

20. Scanning optical microscope of Claim 1, characterized in that light of a plurality of different wavelengths is imaged on one photographic element.

[Field of Technology to which the Invention Belongs]
The invention relates to scanning microscopes, confocal microscopes, fluorescence microscopes and spectral microscopes.

[Prior Art]
There has been a growing demand in recent years for scanning microscopes and confocal microscopes that afford scanning at high speed and observations at high speed. Although hitherto disclosed microscopes include a disk scanner microscope (US5717519) in which the process of tandem scanning is improved and in which, for example, a lens array is employed, using this method, the alteration of the pinhole diameter is difficult and the setting of the optimum confocal diameter in the objective lens is very difficult. Additionally, in this method, the adjustment and centering of a plurality of pinholes and lens arrays is technically difficult. In addition, although, for a sample body in which there is extensive scattering, single-point scanning of the sample body can improve the contrast of the image, the process of changeover from multiple-point scanning to single-point scanning is very difficult.

In addition, although a method for producing an image by the scanning of an array comprising a plurality of focal points in a small range and a method for producing an image in which a plurality of linear laser beams are scanned over a small range have been disclosed (USP6028306), using these methods, the adjustment and centering of a plurality of pinholes and lens arrays is technically difficult. In addition, because a large number of pinholes are present on the entire surface in the field of view, there are times when, in the observation of a sample body that is thick and has extensive scattering, the contrast of the image is reduced due to the scattering of the sample body. In addition, although, for a sample body in which there is extensive scattering, single-point scanning of the sample body can raise the contrast of the image, the process of changeover from multiple-point scanning to single-point scanning is very difficult.

Furthermore, a line scanning confocal microscope described in the Handbook of Biological Microscopy Second edition Chapter 25, page 406, Figure 2(b), has been disclosed and although, using this method, because a line scanner is employed, the confocal effect is increased only in the X direction or Y

direction at one side of the image, because the confocal effect is lowered on the opposing side, the resolution is lower than for a single-point or multiple-point confocal microscope. In addition, the implementation of line sequence scanning in which the scanning excitation wavelength is altered for each wavelength is very difficult. In addition, the image magnification cannot be altered easily without the employment of a relay system and, furthermore, the setting of the optimum scanning speed for the sample body is difficult.

In addition, although a two-photon microscope has been disclosed in which an MMM (Multi-color Multi-focal Multi-photon, Stefan W. Hell, US6262423) is employed, the microscope of this configuration does not comprise a confocal diaphragm. In addition, because the adoption of a configuration in which a confocal diaphragm is inserted into the microscope is difficult, the improvement of this method by the production of a confocal point is very difficult.

In addition, although a video rate scanning microscope has also been disclosed in which an AOTF is employed (US4893008), aberrations are produced when this microscope is used due to the effect of the AOTF on the laser beam itself which ejects the AOTF. As a result, there are times when the resolution is inferior to that of a point scanner-type laser scanning optical microscope.

In addition, in point scanner-type laser scanning microscopes that employ a galvanometer mirror, because the sample body cannot be scanned at a plurality of points and the galvanometer mirror cannot be shaken at high speed, the scanning speed is very slow (Handbook of Biological Microscopy Second edition Chapter 9, pages 139-154).

In addition, although scanning microscopes that use an oscillating galvano have previously been disclosed, the scanning speed cannot be freely controlled using an oscillating galvano. This is a particular difficulty even when the scanning is slow and even when the photometry position is fixed for the implementation of the photometry of a single-point light.

In addition, hitherto devised single-point scanning confocal microscopes as disclosed in US6069734 cannot accommodate objective lenses of large pupil diameter. In response to this, a galvanometer mirror comprising a mirror of large diameter must be adopted but, because the scanning of a large diameter galvanometer mirror at high speed is very difficult, the actualization of high speed scanning has, to this point, proven difficult.

Although micro-mirrors are employed in the present invention, the confocal image projected on to the photographic element which is, strictly speaking, a point light, dot light or line-shaped light rather than an image, does not

constitute a two-dimensional image. To that end, the present invention is fundamentally different to the methods of observation that employ a DMD such as disclosed in US5597832, US5923466 and US 6038067)

[Problems to be Solved by the Invention]

There is expectation that the confocal microscope will fulfill the following conditions:

(1) Able to work at a high-speed scanning speed.
(2) Able to produce high resolution by the generation of a confocal effect in both the X and Y directions of the image.
(3) Diameter of the confocal diaphragm can be altered easily.
(4) Changeover between single-point scanning, multiple-point scanning and line scanning is possible.
(5) Reflected light observation and fluorescence observation is possible.
(6) Fluorescence observation can be achieved by multi-photon excitation such as two-photon and three-photon excitation.
(7) Can be used with normal objective lens and objective lens of large pupil diameter.
(8) Reflected light, transmitted light, fluorescence, non-linear light and Raman spectral data can be obtained from the sample body.
(9) Light images such as SHG (Second Harmonic Generation), THG (Third Harmonic Generation), CARS (Coherent Anti-Stokes Raman Scattering) and Raman can be produced.

Using the confocal microscopes of the prior art the mere co-existence of the two points of (1) "High speed scanning speed" and (2) "Generation of the confocal effect in both the X and Y directions of the image" has been difficult to achieve.
Moreover, the simultaneous fulfillment of the above-noted nine conditions has been extremely difficult.

[Means to Solve the Problems and Action]

Hitherto, if there has been a desire to produce an image scanned at high speed by the employment of a single-point illumination method confocal microscope that employs a galvanometer mirror, because the image cannot be produced unless the voltage of the PMT (multiplier phototube) is increased significantly, the images that have been formed have possessed a marked level of fuzz. In addition, although an image with clear illumination at high speed and which is clearer than that obtainable using a single-point illumination method confocal microscope is produced when a line scanning confocal microscope is employed, the confocal effect, as with the single-point

illumination method confocal microscope, can only be produced in one of either the X or the Y direction of the image.

Thereupon, by the adoption of a scanning optical microscope characterized in that it is configured from an illumination light source, a lens member necessary for altering the cross-sectional shape aspect ratio of the beam of light emitted from the light source, at least one lens for converging beams of light of different cross-sectional shape aspect ratio to create a linear light, a light modulation member able to impart shade to the converged linear light; at least one lens that can form the light to which the shade has been imparted as a parallel light, at least one scanning member that can alter the angle of illumination, at least one lens for imaging the light to which the shade has been imparted in one action, an objective lens that is employed to guide the light to which the shading has been imparted to a sample body, a member which can impart a confocal effect on the light which has returned from the sample body, at least one lens necessary for imaging the reflected light from the sample body or the light generated from the sample body on to a line sensor, photographic element or light-receiving element, along with a line sensor, photographic element or light-receiving element, high speed scanning speeds and a confocal effect in both the X and Y directions of the image can be produced.

This scanning optical microscope is further characterized by the employment of a laser beam or a white light source such as a high-pressure mercury lamp, xenon lamp, halogen lamp or metal halide lamp as the illumination light source. The illumination light source can be designed to deal with a variety of light sources by, simply, the alteration of the optical system between the light source and an element for separating the illumination light and the observed light from the ejection end of the fiber that has connection to the light source (beam splitter), by way of example, a dichroic mirror, AOD, holographic notch filter, glass plate or half mirror.

Furthermore, using a conuter [sic], the start and stop operations of the scanning member and the regulation of the scanning speed thereof can be implemented, the illumination pattern of the light modulation member can be altered, and the ON/OFF irradiation of the illumination light on the sample body can be controlled. As a result, the sample body can be scanned in a variety of patterns. By way of example, the sample body can be single-point scanned, the sample body can be multiple-point scanned, the sample body can be scanned in lines, and light can be made to fall incident on just one segment of the sample body.

Furthermore, if a high sensitivity cooled CCD camera, back-illuminated CCD camera or cascade camera, or CCD camera with an image intensifier or the

like are employed as the photographic element, very weak light can be captured.

Furthermore, by the scanning of the illumination light using a galvanometer mirror and by the timed shifting of a single-point illumination light employing a mirror or diaphragm of a size that achieves the resolution limit of the light modulation member in which the shade pattern is alterable, a confocal diaphragm effect can be generated in both the X and Y directions of the image.

Furthermore, where scanning of the sample body at high speed is desired, by the illumination of the sample body by the imparting of a pattern of alternating shade at each single point on the light modulation member in which the shade pattern is alterable and, furthermore, the shifting of this shade pattern, a plurality of points can be simultaneously illuminated so that a confocal diaphragm effect can be generated in both the X and Y directions of the image and, furthermore, so that the image can be photographed at high speed.

Furthermore, if scanning at high speed is desired and, if line-scanning illumination is implemented, the line scanning confocal microscope can be actualized in such a way that the light modulation member in which the shade pattern is alterable can be linearly illuminated.

Furthermore, if a lowering of the confocal effect or the imparting of bright illumination is desired, the same effect as the effect obtained when the confocal diaphragm is opened can be produced by the employment of a mirror or diaphragm of a surface area that is significantly larger than the resolution limit for a single point of the light modulation member in which the shading pattern is alterable, or by the simultaneous transmission or reflection thereof through the adjacent plurality of mirrors or diaphragms.

Furthermore, there are times when, even in the use of a confocal microscope, the observation of an image of depth as deep as that for a reflecting microscope or fluorescence microscope is desired. Hitherto, it has been very difficult to actualize confocal microscopes. In the present invention, because a two-dimensional element is employed as the light modulation member in which the shade pattern is alterable and the laser light can be led to the whole of the sample body surface and, furthermore, the image of the sample body can be projected, unaltered, on to the photographic element by the scanning of the scanner to illuminate the illumination light across the whole field of view, the reflected light and fluorescence of a normal sample body can be observed.

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Furthermore, in addition to the single-photon excitation fluorescence observation which has hitherto made observation possible, a demand has arisen for fluorescence image observation which, based on multi-photon excitation such as two-photon excitation or three-photon excitation, uses a femto-second laser or the like such as a titanium sapphire laser. Observation of the fluorescence image is possible in the present invention using two-photon excitation or three-photon excitation by the employment of, for the production of the illumination light, an ultra-short pulse light source such as a titanium sapphire laser.

Additionally, although there are times when spectral diffraction of the fluorescence or reflected light from the sample body is desired, this is difficult using the hitherto employed techniques. Using the present invention, a spectral device can be configured by the insertion of a spectral diffraction element which employs a diffraction grating or Acousto-Optic Modulator (AOM) between the photographic element and the light-strength modulation member, and by having, for example, a CCD camera that constitutes a two-dimensional photographic element. If an Acousto-Optic Modulator is employed, the changeover between spectral measurement and normal measurement can be implemented by the turning ON and OFF of an electrical switch.

In addition, if an ultra-short pulse light source is employed, reception of non-linear light generated from the sample body, by way of example, secondary harmonic, tertiary harmonic, Raman light, and CARS (Coherent Anti-Stokes Raman Scattering) is possible. In this case, the optical characteristics of the part for dividing the illumination light and the received light of the present invention, and with the band pass filter or spectral element provided in front of the light-receiving element, must be optimized. The part for dividing the illumination light and the received light refers to, for example, a dichroic mirror for reflecting the illumination light, or, a holographic notch filter to which the illumination light is led, which are provided between the light source and the light strength light modulation member. In addition, the band pass filter or spectral element provided in front of the light-receiving element constitutes an Acousto-Optic Modulator AOM or interference filter for restricting the range of the wavelength of the light received and is inserted between the tight reception element and the part for dividing the illumination light and the received light. For CARS (Coherent Anti-Stoke Raman Scattering), the illumination must be performed using different ultra-short pulse light sources with two wavelengths.

In addition, if the ON and OFF of the light modulation member and the synchronization of the galvanometer mirror are used properly the light can be irradiated only on the prescribed position of the surface of the sample body. In addition, if a laser that produces a plurality of wavelengths is employed as the

light source the illuminated wavelength can be changed over, or, if a mercury lamp, xenon lamp, metal halide lamp and halogen lamp or the like is employed, the light generated from these light sources can be selectively irradiated on the sample body. By virtue of this, the scattering of a fluorescent pigment can be observed by, for example, employing dyed cells or cell groups as the sample body and causing one part of said cells to fade. If protein is imparted to the pigment, the diffusion of the protein can be seen at high speed. In addition, if a caged compound is employed, localized increases in the concentration of the calcium and the like are possible. For example, light which introduces caged calcium into the sample body of the cells or cell groups and the like and which releases caged [sic] to specific parts of the cells is irradiated. Although, by way of example, a means has been disclosed for the measurement of changes of a cell that follows the localized increase of the density of the calcium, the present invention can also accommodate the tests and observations such as this.

A summary of the fundamental essence of the present invention is given below.

Light from a light source is linearly converged to fall incident on a light strength modulation element such as a DMD or liquid crystal. Next, following the modulation of the linear light by the light strength modulation element into a light with a prescribed shade along the direction of the rays thereof, the light is irradiated on the sample body. The light generated from the sample body (reflected light and fluorescent light and so on) is returned to said light strength modulating member, after which it is separated from the illumination optical path and detected by a light detection element. Examples of the light-detecting element that is employed include a one-dimensional line sensor and a two-dimensional CCD camera.

The "bright" sections of the linear light comprising the shade patterns are, while being successively moved, sequentially detected by the light detection element, and the detected images correspondent to each of the shade patterns are accumulated. Following this, the detected images of the single segments are synthesized in the final step.
To form a two-dimensional picture, the linear light is scanned using a galvano mirror or the like.

[Embodiment Mode of the Invention]
The configuration thereof is as outlined below.
A description is given of a first Embodiment. Figure 1(a) represents a diagonal view of the optical system of this device, and Figure 1(b) represents the view thereof from above. The illumination in the configuration of the device of the present invention is implemented by the employment of a laser. If a continuous oscillating laser is employed the light can be introduced into

the device by way of a single mode fiber. The introduced light is formed as a parallel light beam by a collimator lens. If a laser for oscillating an ultra-short pulse light, by way of example, of a femto-second, is employed, the light can be introduced by the employment of a hollow fiber. If the employment of a hollow fiber is undesirable, the laser light may be introduced directly to the device.

The introduced laser passes through a lens 3, which constitutes a lens necessary for altering the cross-sectional shape aspect ratio of the beam which is configured from at least one cylindrical lens or at least one fθ lens, and is converted to a laser light in which the cross-sectional shape aspect ratio of the beam is different. It is desirable that the color aberrations are corrected so that the cylindrical lens or the fθ lens and so on can accommodate a broad range of wavelengths. Laser light in which the cross-sectional shape aspect ratio of the beam is different can be more brightly illuminated on the object surface than expanded laser illumination because it is a linear infinite beam possessing a degree of width.

The laser light in which the cross-sectional shape aspect ratio of the beam is different falls incident on and is reflected from a beam splitter 15. The beam splitter 15 is configured from a dichroic mirror, or half mirror of a reflecting ratio of the order of 50–2%, or a glass plate that reflects a small amount of the illumination light. The light then falls incident on a lens 2 which constitutes a laser converging lens configured from at least one lens for converging laser light in which the cross-sectional shape aspect ratio of the beam is different. The light ejected on to the lens 2 is converged and formed as a linear light. In addition, the lens 2, in such a way that it can linearly converge light of a plurality of different wavelengths on the same position, requires that the color aberrations have been corrected.

The converged linear laser light falls incident on a light modulation member 4 for implementing modulation in such a way as to comprise sections of bright strength and sections of dark strength, whereupon it is transmitted or reflected. The light modulation member 4, which comprises a plurality of small reflection mirrors, may employ a DMD (Digital Mirror Device) that is characterized by the switching ON and OFF of each small reflecting mirror, or an SLM (spatial light modulator) or a liquid crystal plate able to change the transmissivity. A DMD is employed in Embodiment 1. When each of the small reflection mirrors are switched ON by the DMD the light that falls incident on the mirrors is reflected to the optical path of the microscope (lens 1 side) and, when it is turned OFF, the light is reflected in a direction away from the optical path of the microscope. Accordingly, by the ON and OFF control of the small mirrors, the light that falls incident on the DMD is modulated from a converged linear laser light to a linear laser light in which a shade pattern has been imparted, or it is reflected. If a liquid crystal plate is used, the light that

falls incident on the liquid crystal plate can be modulated to a linear laser light in which a shade pattern has been imparted due to the changes in the transmissivity produced as it is transmitted through the liquid crystal plate.

The linear laser light in which a shade pattern has been imparted falls incident on a lens 1 which constitutes a lens for converting light to a parallel light with width, and dot light, which is formed as a parallel light with width, falls incident on a galvanometer mirror 5. The galvanometer mirror 5 has the role of altering the angle of the parallel light with width over time by the shaking of said mirror. After passing through a pupil lens 6, the parallel light with width is re-imaged at a position 7 between the pupil lens and an imaging lens. It is desirable that the color aberrations be corrected in such a way that the pupil lens 6 can accommodate a broad range of wavelengths.

The linear laser light to which the shade pattern has been imparted and which is transmitted through the pupil lens to be re-imaged at a position 7 between the pupil lens and an imaging lens, is transmitted through an imaging lens 8 and imaged on the sample body surface 10 by an objective lens 9.

The light imaged on the sample body surface is reflected or converted to fluorescence by a fluorescence generating material to be transmitted through the objective lens whereupon, after further transmission though the imaging lens 8, it is imaged at a primary image surface position 7, transmitted through the pupil lens 6 to be reflected by the galvanometer mirror, caused to fall incident on the lens 1, imaged on a light strength modulation member 4 which constitutes a secondary imaging surface, and reflected or transmitted by the light strength modulation member 4. The light strength modulation member 4 fulfils the role of a confocal diaphragm. The light which is reflected or transmitted by the light strength modulation member 4 is formed as a parallel light by the lens 2, and is transmitted through a beam splitter 15 configured from a dichroic mirror, a half mirror or a glass plate, and is transmitted through a lens 11 and imaged on a photographic element 12.

A laser light source 13, which is able to employ a single wavelength laser, may also employ an irradiating laser of a plurality of wavelengths. For a laser of a plurality of wavelengths either an argon laser or krypton/argon laser that emits a plurality of wavelengths or a laser combiner in which a plurality of laser are combined can be employed. If a laser of a plurality of wavelengths is employed, an AOTF (Acousto-Optical tunable filter) can be employed so that only the target wavelength is selected.

By virtue of the fact that the photographic element 12, the light strength modulation member 4 and the galvanometer mirror 5 are connected to a computer 90 by, respectively, a photographic element control part 121, a DMD driver 41 and a galvano mirror driver 51 and they can be mutually linked

and driven, a picture image can be formed. In addition, a monitor 91 is connected to the computer 90, and the picture image formed by the computer 90 is displayed on this monitor 91.

If the confocal microscope of Embodiment 1 is employed and single-point illumination of the sample body is performed, the flow of the process that is implemented is as shown in Figure 2 (a). In reality, a DMD configured from a plurality of mirrors of 1024 x 768 pixels or 1280 x 1024 pixels is employed but, in Figure 2, a description of the principles thereof is given using a virtual DMD configured from a 9 x 8 pixel mirror. The illumination light is irradiated by a lens 2 on to a DMD that constitutes the light strength modulation member 4. The illumination light constitutes a linear light ray as shown by 51. A mirror 56, which is ON, initially reflects the illumination light and then, by way of a lens 1, the light is reflected by the galvanometer mirror 5 and led to the sample body 10. At this time, because all mirrors other than the mirror 56 are in the OFF state, the light reflected by the OFF section is not led to the sample body. Next, when the mirror 56 is switched OFF the mirror 57 is switched ON. The illumination light is reflected by the mirror 57 and then, by way of the lens 1, is reflected by galvanometer mirror 5 and led to the sample body 10. The changeover of the ON position and sequential illumination from the mirror 56 to the mirror 64 is performed in such a way that the illuminated light appears to be scanned in the X-axis direction of the DMD. In addition, when the illumination of one line segment on the X-axis has been completed, the galvanometer mirror is then shifted one line in the Y-direction where the further sequential illumination from the mirror 56 to 64 of the DMD is performed, and this is again followed by the shift of the galvanometer mirror another one line in the Y-direction. Single-point scanning confocal illumination can be performed by the sequential implementation of this operation and illumination to the last line in the Y direction.

This series of cooperative actions is implemented by the control of the computer 90.
The computer 90 has the function of a pattern control part for determining the illumination pattern of the line-shaped light as shown in Figure 2 (a) to Figure 2 (i).
In addition, the computer 90 comprises a function as a picture forming part whereby, by the accumulation of the acquired line image data correspondent to each illumination pattern in the inner part memory of the computer and the synthesis thereof, it forms one observed picture image.
The computer 90, by the acquisition of the shade patterns of the light irradiated on the sample body from the pattern control part for determining the shade patterns of the line-shaped light, and the re-arrangement of this acquired line image data in accordance with the illumination pattern, creates a two-dimensional picture image of the sample body. More specifically, by way of example, only the line image data equivalent to the "bright" section in the

shade pattern is adopted as the luminance data for said position, and the line image data when the light has been sequentially irradiated in different shade patterns is processed and rearranged in the same way. Provided the confocal illumination is implemented at all pixel positions on a single picture section, one confocal picture image is formed by the rearrangement of the line image data acquired by this method.
Or, without this rearrangement, a two-dimensional confocal image can be formed if the acquired line image data for identical lines is added together.

In addition, if there is a desire for observation which involves, instead of enlarging the diameter of the confocal diaphragm which reduces the resolution, the brightening of the brightness, a plurality of adjacent mirrors as shown in Figure 3 (a) are switched ON. By way of example, an effect identical to that obtained when the confocal diaphragm is opened will be produced if mirrors 81, 82, 83 and 84 are simultaneously switched ON. If the focal distance of the lens 3 is optimized in such a way that the illumination light can be irradiated in a broad range as shown by 80, both the illumination range and light-receiving range can be simultaneously controlled by the light strength modulation member. In addition, even in a configuration in which the focal distance of the lens 3 is regulated and the illumination range that can be produced constitutes the illumination produced by the stopping of the illumination light as shown by 51 of Figure 2, because the effect on the observed image is as if the confocal diaphragm was expanded if the mirrors 81, 82, 83 and 84 are simultaneously switched ON as shown in Figure 3, the image is brightened. For scanning, as shown in Figure 3 (b), the mirrors 81, 82, 83, 84 are switched OFF and the mirrors 85, 86, 87, 88, which constitute an adjacent group, are switched ON. The scanning in the X-direction is implemented by the sequential switching ON of the plurality of adjacent mirrors in this way. By implementation of the scanning in this way, an identical effect to that achieved when the confocal diaphragm is expanded can be produced and a bright image can be produced.

A description is given below of a method for the illumination of a sample body at a plurality of points by the imparting of shade to a linear illumination light. The description in this case is also given with reference to Embodiment 1. The illumination light is illuminated by the lens 2 on to a DMD that constitutes a light strength modulation member 4. Furthermore, one part of the DMD is shown in Figure 4. The illumination light constitutes a linear light ray as shown by 90 of Figure 4 (a, b). The linear illumination light is irradiated on a section in which a plurality of mirrors is alternately switched ON and OFF as shown in Figure 4(a). The illumination light is converted to a dot linear light from linear light by the plurality of mirrors. Next, the dot light is projected on to the sample body surface. Furthermore, the illumination light is illuminated across the whole of the observation range of the sample body 10 by a scanning of the galvanometer mirror 5 correspondent with the Y-axis. The light that is

reflected or converted to fluorescence by the sample body 10 is reflected again by the galvanometer mirror 5, transmitted through the lens 1, and imaged on the DMD light strength modulation member 4. The plurality of mirrors in the ON state on the DMD fulfills the role of the confocal diaphragm. The light that is transmitted through the plurality of mirrors in the ON state is imaged on the photographic element 12. This imaged image is sent to the memory of the computer 90 as image data 100. Next, linear illumination light is irradiated on to a plurality of mirrors set in a reverse pattern to the ON and OFF pattern as shown in Figure 4 (a). This DMD state is shown in Figure 4 (b). When the illumination light is irradiated on to the plurality of mirrors for which the OFF and ON has been alternately set, the illumination light is converted from a linear light to a dot shape by the plurality of mirrors. The dot light is projected onto the sample body surface. When the DMD mirrors are set as shown in Figure 4 (a) the dot illumination light is illuminated on to the sample body as dot rays in which the illumination has been reversed. Furthermore, the illumination light is illuminated across the whole of the observation range of the sample body 10 by the scanning of the galvanometer mirror 5 correspondent with the Y-axis. The light reflected or converted to fluorescence by the sample body 10 is reflected again by the galvanometer mirror 5, transmitted through the lens 1, and imaged on the DMD light strength modulation member 4. The plurality of mirrors in the ON state on the DMD fulfills the role of the confocal diaphragm. The light that has been transmitted through the plurality of mirrors in the ON state is imaged on to the photographic element 12. This imaged image is sent as image data 101 to the memory of the computer 90. The image data 100 and image data 101 are synthesized by the computer 90 to produce a final picture image 102.

In addition, if a desire exists for the pictures to be taken at higher speed than for single-point scanning and, because scattering exists in the sample body and a desire exists to reduce the deterioration of the image due to this scattering, the interval between the ON and ON of the DMD can be increased in multi-point scanning. The setting of the DMD in this case is shown in Figure 5. In this case, by way of example, the switch for the DMD is set so that a plurality of OFF, that is, ON, OFF, OFF, ON, exist between the ON. The number of OFF to be set between one ON and the next ON is determined by the thickness of the sample body and the amount of scattering. For a sample body in which there is a large amount of scattering, it is desirable that a large number of OFF be provided between one ON and the next ON. First, as shown in Figure 5 (a), a repeating pattern of ON, OFF, OFF is set and the sample body 10 is scanned by the galvanometer mirror 5 to produce image data 105 from the photographic element 12. Next, as shown in Figure 5 (b), a pattern of OFF, ON, OFF is set and the sample body 10 is scanned by the galvanometer mirror 5 to produce image data 106 from the photographic element 12. Furthermore, as shown in Figure 5 (c), a pattern of OFF, OFF, ON is set and the sample body 10 is scanned by the galvanometer mirror 5 to

produce image data 107 from the photographic element 12. Using the computer 90, the image data 105, 106 and 107 is synthesized to produce final picture image data 108.

In addition, if a desire exists for the pictures to be taken at higher speed than for single-point scanning and, because scattering exists in the sample body and there is a desire to reduce the deterioration of the image due to this scattering and to simultaneously brighten the image, a plurality of OFF can be provided in multi-point scanning between one ON and the next ON of the DMD and, as far as the ON itself is concerned, a plurality of continuous ON can be set. This example is shown in Figure 6. The setting of the mirrors here is ON, ON, OFF, OFF, OFF, OFF. By the adoption of this setting the brightness and contrast of the image can be increased and the image can be produced at comparatively high speed.

In addition, a description is given below, with reference to Figure 7, of the taking of the picture of a spectral picture image using the device of Embodiment 1. In Figure 7, in addition to the photographic element 12 of the confocal microscope of the configuration identical to that of Figure 1, a two-dimensional sensor, by way of example, a CCD camera, is employed, and a spectral element 14, by way of example, a diffraction or Acousto-Optic Modulator (AOM), is provided between the photographic element 12 and the light strength modulation member 4.
The spectral element 14 is arranged in such a way that spectral diffraction of the linear (dot ray) light that falls incident on the spectral element 14 occurs in the direction orthogonal to the direction of the rays.
If a diffraction element is employed as the spectral element 14, changeover from the spectral confocal microscope to a normal confocal microscope can be achieved by the operation of the provision and removal of the element in the optical path. In addition, if an Acousto-Optic modulator is employed, use as a spectral confocal microscope is possible if the Acousto-Optic element is switched ON and, if the element is switched OFF, without a driving part, changeover to a normal confocal microscope is possible. Figure 8 represents an example of a spectrum for a case in which the sample body has been illuminated by an illumination light possessing shade. The X-axis direction of the observed image photographed by the photographic element 12 (CCD camera) is correspondent to the pixel position in the X-direction and the Y-axis direction thereof corresponds to the wavelength. The luminance of the pixels in the picture image expresses the strength of the light for each wavelength in the pixel position in the X-direction.

Not only a point source such as a laser but also a so-called white light source, for example, a mercury or xenon lamp or halogen lamp, can be employed in this optical system. In this case, there are no limitations to the wavelength that can be illuminated on the sample body. This is particularly effective if the

present invention is employed as a fluorescence microscope because excitation at a variety of wavelengths is possible.
In Figure 9, which depicts a device in which a plurality of photographic elements are employed, the light from the sample body is separated for each wavelength by dichroic mirrors 16a to 16c so that the light of these respective wavelengths can be simultaneously photographed.

In Figure 10, which depicts a configuration in which a diffraction optical element, by way of example, a holographic notch filter or Acousto-Optic Modulator is employed, the optical path of the excitation light only is refracted causing the illumination light to fall incident from the lateral direction. If a configuration such as this is adopted, all wavelengths other than that of the excitation light can be led to the photographic element whereby the illumination can be achieved with higher efficiency than is obtainable with the dichroic mirrors and a sample body with little Stokes shift can be observed.

Figure 11 shows an example configured from a liquid crystal diaphragm in which no DMD is employed in the light strength modulation member.
This liquid crystal diaphragm, in the same way as the DMD, implements a changeover control involving the transmission (ON) or non-transmission (OFF) of the light that falls incident based on a unit size of the order of the resolution limit. By virtue of this, the liquid crystal diaphragm fulfils a function of modulating the light strength of the linear light. In the same way as Embodiment 1, the galvano mirror and photographic element are linked and controlled by the computer 90.

Figure 12 shows an example in which fringes are formed and fringes are projected on the sample body by the provision in the illumination light of a diffraction grating, the single refraction of the illumination light, and the obstruction of the + 1 primary light or −1 primary light of the diffracted light. Because the fringes are displaced if the + 1 primary light or −1 primary light are obstructed, a description will be given of the principles thereof. If this illumination method is employed, a confocal effect can be produced in the X-direction of the image by the employment of a light strength modulation member such as a DMD and, as disclosed in US 6376818, a confocal effect can be produced in the Y-direction of the image by the projection of these fringes.

Figure 13 is a diagram that shows the diffraction grating, lens 17, 18, and a liquid crystal shutter 19.

In addition, in order to detect a bright image using this optical system, the system must be able to accommodate objective lenses of large pupil diameter. Although the NA in the light ray ejection for the imaging of the primary image of a sample body in hitherto employed microscopes is of the

order of 0.03, to be able to observe a bright image across a wide range, the system must be able to accommodate NA values of between 0.04 to 0.1 or greater, by way of example, a value of 0.175. In an optical system comprising a pupil of large diameter such as this, a large diameter galvanometer mirror must be adopted. The driving of a galvanometer mirror of large diameter such as this at high speed is difficult. Although, in order to take an image of resolution 512 x 512 using the confocal microscopes of the prior art in which XY scanning is implemented using a galvanometer mirror, at least the X-scanning galvanometer mirror must be shaken 512 times, because an X-scanning galvanometer mirror is unnecessary in the confocal microscope of this configuration and the Y-scanning galvanometer mirror need be shaken only once, pictures of the image can be taken at high speed even if a comparatively large galvanometer mirror is used.

Description of Figure 15. If the ON and OFF of the optical modulation member and the phase of the galvanometer mirror are properly used, the light can be irradiated on specified positions on the surface of the sample only. A description is given below of the means employed for this at this time. Figure 15 shows pixels that correspond to cells 111 on the sample body and the range 112 across which the taking of pictures is possible. Here, a description is given of a method for observing a fluorescence image in which light is irradiated on to one part 110 of these cells.

1. The illumination light is set at the desired illumination wavelength.
2. All mirrors of the DMD element, which constitute the light strength modulation member 4 and which correspond to X1 to X11 in the Y1 line, are switched OFF.
3. The galvanometer mirror, for which alteration of the illumination position in the Y-axis can be performed, is moved from a position in which Y1 can be illuminated to a position in which Y3 can be illuminated.
4. Light is irradiated by the switching ON of the DMD correspondent to the illuminated position X5, X6 of the line Y3 only.
5. The galvanometer mirror is moved, X5, X6 of the line Y4 are illuminated, and X5, X6 of the line Y5 are illuminated.
6. The DMD correspondent to the X5, X6 position of the line Y5 is changed over to OFF, and the galvanometer mirror, by way of the position Y6, is shifted to the position Y10.
7. If there is a desire for the scanning to be implemented several times, the operations from 2 to 6 can be repeated.
8. The taking of the pictures of the fluorescence image is initiated.

Description of Figure 16. Figure 16 shows an example in which a one-dimensional Digital Mirror Device array, in which mirrors are arranged in a line in the light strength modulation member 4, is employed. The configuration adopted in this embodiment is one in which the optical path is caused to bend upward from the galvano mirror 5. Although not shown in the configurations of

the embodiment of Figure 1, Figure 7, Figure 10, Figure 11, Figure 12 and Figure 14, the adoption of a configuration in which the optical path bends upward from the galvano mirror 5 is also possible. As the photographic element of Figure 16, a line sensor is employed. In the confocal observation of all the embodiments, a line, dot or dot ray is projected on to the photographic element 12.

Description of Figure 17.
By the adoption of a scanning optical microscope configured from an illumination light source, a lens member necessary for altering the cross-sectional shape aspect ratio of the beam of light emitted from the light source, at least one lens for converging beams of light of different cross-sectional shape aspect ratio to create a linear light, a light modulation member able to impart shade to the converged linear light, at least one lens that can form the light to which the shade has been imparted as a parallel light, at least one scanning member that can alter the angle of illumination, at least one lens for imaging the light to which the shade has been imparted in one action, an objective lens that is employed to guide the light to which the shading has been imparted to a sample body, at least two lens necessary for imaging the reflected light from the sample body or the light generated from the sample body on to a line sensor, photographic element or a light-receiving element, or one lens and light-receiving element for imaging a plurality of focal points using one lens, light of a plurality of wavelengths can be projected on to one two-dimensional photographic element. By the adoption of a configuration such as this, because pictures of an image of at least two wavelengths can be simultaneously taken using one CCD, the device can be configured inexpensively.

In Figure 17, by the division in two of the light led from the sample body by a dichroic mirror 151, the passing through band pass filters 152, 155 through which the respective lights of different wavelength are transmitted and, furthermore, the reflection by mirrors 153, 156 and the imaging by imaging lenses 158, 159 respectively, two different lights can be projected on to the one photographic element. By the adoption of a configuration such as this, two images can be produced using one two-dimensional photographic element. Although the configuration in this embodiment is one in which two different wavelengths are projected, in actual practice, a configuration can be adopted in which light of two or more wavelengths is projected.

Figure 18 shows an example in which two line shaped lights 160, 161 from mirrors 156, 158 are juxtaposed in the lateral direction and received by a photographic element 157. Figure 19 shows an example in which two line shaped lights 162, 163 from the mirrors 156, 158 are juxtaposed in the vertical direction (up/down direction in the diagram) and received by the photographic element 157. When the light is received in two lines in the

up/down direction of the photographic element as shown in Figure 19, the light of two wavelengths can be received without reduction in the resolution of the image.

Using the present invention, a picture image can be produced that is not confocal. By the employment of a two-dimensional element as the light modulation member in which the shade pattern is alterable, the leading of the whole of the laser light to the sample body surface and, furthermore, the scanning of the galvanometer mirror to irradiate the illumination light across the entire field of view, the light from the sample body, using a photographic element, can be produced as an image. By way of example, when the embodiment of Figure 1 is employed, if the laser 13 is irradiated and all of the light modulation member 4 is switched ON to scan the galvanometer mirror 5 and illuminate the sample body, the reflected light, fluorescence and light generated from the sample body will be reflected again by the galvanometer mirror 5 and, by way of the light strength modulation member 4, is led to the photographic element 12. As a result, the reflected light or fluorescence of a normal sample body can be observed.

Examination of the Prior Art
As a result of the search carried out in the US around the terms "slit AND scan AND confocal AND image", 140 patents were found. No similar technology was uncovered therein.
Prior art examples
US561554, US5153428, US5633751, US5717519, US5579157, US6031661, US6262423, US4893008, US6028306, US6069734, US6144489, US6376818, US6108081, US4405237, US5587832, US5923466, US5034613, US6134002, US5751417 and US5248876
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The Intermediate Optical System of Laser-Scanning Confocal Microscopes, Ernst H. K. Stelzer, Handbook of Biological Microscopy Second edition Chapter 9, page 139-154
Direct View Confocal Imaging Systems Using a Slit Aperture, W.B. Amos and J.G. White, Handbook of Biological Microscopy Second edition Chapter 25, page 403-415

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